

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

Claims 1-30 (canceled)

Claim 31 (currently amended): A polynucleotide microarray hybridizing to first and a second labeled DNA portions, wherein the portions are from uniform populations of randomly cleaved or sheared DNA from a cell or organism;

wherein the first DNA portion comprises unmethylated and methylated DNA labeled with a first label; and

wherein the second DNA portion is depleted for either unmethylated DNA or methylated DNA and the second portion of DNA is labeled with a second label different from the first label.

Claim 32 (original): The polynucleotide microarray of claim 31, wherein the second test DNA portion is depleted for methylated DNA.

Claim 33 (original): The polynucleotide microarray of claim 31, wherein the second test DNA portion is depleted for unmethylated DNA.

Claim 34 (currently amended): The polynucleotide microarray of claim 31, wherein the second DNA portion is depleted by

treating the randomly cleaved or sheared DNA with a methyl-sensitive or a methyl-dependent restriction enzyme and

selecting ~~uncleaved~~ DNA not fragmented by the restriction enzyme.

Claim 35 (original): The polynucleotide microarray of claim 31, where the DNA populations are from a plant.

Claim 36 (original): The polynucleotide microarray of claim 31, where the DNA populations are from an animal.

Claim 37 (original): The polynucleotide microarray of claim 31, where the DNA populations are from a fungus.

Claim 38 (original): The polynucleotide microarray of claim 31, where the DNA populations are from a prokaryote.

Claim 39 (original): The polynucleotide microarray of claim 38, wherein the prokaryote is a bacterial pathogen.

Claim 40 (original): The polynucleotide microarray of claim 39, wherein the bacterial pathogen is selected from the group consisting of *Listeria*, *E. coli*, *Salmonella*, *Yersinia*, and *Neisseria*.

Claim 41 (currently amended): The polynucleotide microarray of claim 31, where the DNA populations are from a transgenic organism, or cell, or tissue.

Claim 42 (original): The polynucleotide microarray of claim 31, the polynucleotide microarray comprises gene promoters and/or polynucleotide sequences which when methylated, silence neighboring gene expression.

Claim 43 (currently amended): A method for producing an epigenetically uniform or diverse population of progeny from one or more parent individuals, the method comprising the steps of:

- a. determining ~~the~~ a genomic methylation profile of sexually or asexually propagated progeny of a parent individual; and
- b. selecting progeny exhibiting a uniform or diverse methylation profile, thereby producing an epigenetically uniform population from one or more parent individuals.

Claim 44 (currently amended): The method of claim 43, further comprising determining a the methylation profile of the parent individual and the selecting step comprises selecting progeny that exhibit the methylation profile of the parent individual.

Claim 45 (original): The method of claim 44, wherein the parent is an F1 hybrid.

Claim 46 (original): The method of claim 43, wherein the progeny are sexually propagated.

Claim 47 (original): The method of claim 43, wherein the progeny are asexually propagated.

Claim 48 (currently amended): The method of claim 43, wherein the parent individual is selected from the group consisting of a plant, an animal, a fungus and a prokaryote.

Claims 49-51 (canceled)

Claim 52 (original): The method of claim 43, wherein the progeny are clones of the parent.

Claim 53 (original): The method of claim 43, wherein the genomic methylation profile is determined on a solid support.

Claim 54 (currently amended): The method of claim 53, wherein the solid support is selected from the group consisting of a membrane, a methyl binding column, a microarray, a bead, and a matrix.

Claims 55-57 (canceled)

Claim 58 (currently amended): The method of claim 43, wherein the determining step comprises

separating a randomly cleaved or sheared uniform DNA population into methylated and unmethylated fractions;

labeling the methylated or unmethylated ~~fractions~~ fraction with a first label; and

hybridizing the methylated or unmethylated ~~fractions~~ fraction to a nucleic acid.

Claim 59 (original): The method of claim 58, wherein the method further comprises providing total genomic DNA labeled with a second label and hybridizing the total genomic DNA to a nucleic acid, thereby normalizing the signal from the first label.

Claim 60 (currently amended): The method of claim ~~43~~ 58, wherein the randomly cleaved or sheared DNA comprises methylated and unmethylated recognition sequences of a methyl-sensitive restriction enzyme and the depleting step comprises fragmenting ~~cleaving~~ the second portion with the methyl-sensitive restriction enzyme.

Claim 61 (currently amended): The method of claim ~~43~~ 58, wherein the randomly cleaved or sheared DNA comprises methylated and unmethylated recognition sequences of a methyl-dependent restriction enzyme and the depleting step comprises fragmenting ~~cleaving~~ the second portion with the methyl-dependent restriction enzyme.

Claim 62 (original): The method of claim 43, wherein progeny are screened in groups.

Claim 63 (currently amended): A method of associating heterosis with methylation profiles, the method comprising,
crossing individuals to produce progeny;
determining ~~the~~ a methylation profile of the individuals and the progeny; and
comparing a trait of the progeny with the methylation profiles of the individuals,
thereby associating appearance of the trait with a the methylation profile.

Claim 64 (original): The method of claim 63, wherein the individuals are from different heterotic groups.

Claim 65 (new): The method of claim 63, further comprising comparing the methylation profile of a nucleic acid with a copy number of the nucleic acid, thereby determining the contribution to a phenotype of the combination of the methylation of the nucleic acid and the copy number of the nucleic acid.

Claim 66 (new): The method of claim 65, wherein the copy number of the nucleic acid is detected with a microarray.

Claim 67 (new): The method of claim 43, wherein the determining step comprises:

- a. providing a uniformly-sized population of randomly cleaved or sheared DNA from a cell, tissue, or organism, wherein the DNA comprises a first portion and a second portion and each portion comprises methylated and unmethylated nucleotides;
- b. labeling the first portion with a first label;
- c. depleting methylated or unmethylated DNA from the second portion;
- d. labeling the depleted second portion with a second label that is different from the first label;
- e. hybridizing the first portion and the depleted second portion to a nucleic acid;
- f. determining the relative methylation of the complementary nucleic acid fragments in the DNA by calculating the ratio of the two hybridizing labels, thereby determining the methylation profile of the nucleic acid fragments from a cell, tissue, or organism.

Claim 68 (new) The method of claim 43, wherein the determining step comprises:

- a. providing a uniformly-sized population of randomly cleaved or sheared DNA from a cell, tissue, or organism, wherein the DNA comprises a first portion and a second portion and the DNA comprises methylated and unmethylated recognition sequences of a methyl-sensitive or methyl-dependent restriction enzyme;
- b. labeling the first portion of the DNA population with a first label;
- c. fragmenting the second portion with the methyl-sensitive or methyl-dependent restriction enzyme,
- d. depleting methylated or unmethylated DNA from the second portion;
- e. labeling unfragmented DNA from the second portion with a second label that is different than the first label;
- f. hybridizing the labeled DNA from the first and second portions to a nucleic acid; and

g. determining the relative methylation of a nucleic acid by detecting the first and second labels hybridizing to the nucleic acid, thereby determining the methylation profile of the cell, tissue, or organism.

Claim 69 (new) The method of claim 68, wherein the second portion is fragmented with a methylation-dependent restriction enzyme.

Claim 70 (new) The method of claim 68, wherein the second portion is fragmented with a methylation-sensitive restriction enzyme.

Claim 71 (new) A method for determining a methylation profile of a cell, tissue or organism, the method comprising the steps of:

- a. providing a uniform population of randomly cleaved or sheared DNA from the cell, tissue, or organism;
- b. depleting methylated or unmethylated DNA from the randomly cleaved or sheared DNA; and
- c. quantifying the amount of at least one DNA sequence from the depleted methylated or unmethylated DNA, thereby determining the methylation profile of at least one nucleic acid sequence from the cell, tissue or organism.

Claim 72 (new) The method of claim 71, wherein the depleting step comprises:
fragmenting the randomly cleaved or sheared DNA with a methylation-sensitive or methylation-dependent restriction enzyme to produce DNA fragmented by the restriction enzyme and DNA unfragmented by the restriction enzyme; and
separating the fragmented DNA from the unfragmented DNA.

Claim 73 (new) The method of claim 72, further comprising:
labeling the unfragmented DNA with a label;
hybridizing the labeled DNA to a nucleic acid; and
determining the methylation state of the nucleic acid by detecting the labeled DNA hybridizing to the nucleic acid.

Claim 74 (new) The method of claim 71, comprising the steps of:

- a. providing a uniform population of randomly cleaved or sheared DNA from the cell, tissue, or organism, wherein the DNA comprises a first portion and a second portion and each portion comprises methylated and unmethylated nucleotides;
- b. depleting methylated or unmethylated DNA from the second portion; and
- c. quantifying the relative amount of at least one sequence from at least two of the following:
 - the first portion,
 - methylated DNA in the second portion, and
 - unmethylated DNA in the second portion.

Claim 75 (new) The method of claim 74, wherein the depleting step comprises:

- fragmenting the second portion with the methyl-sensitive or methyl-dependent restriction enzyme to produce fragmented DNA and unfragmented DNA; and
- separating the fragmented DNA from the unfragmented DNA.

Claim 76 (new) The method of claim 75, further comprising:

- labeling the first portion with a first label;
- labeling the unfragmented DNA from the second portion with a second label that is different than the first label;
- hybridizing the labeled DNA from the first and second portions to a nucleic acid;

and

- determining the relative methylation of a nucleic acid by detecting the first and second labels hybridizing to the nucleic acid, thereby determining the methylation profile of at least one nucleic acid sequence from the cell, tissue, or organism.

Claim 77 (new) The method of claim 75, wherein the second portion is fragmented with a methylation-sensitive restriction enzyme.

Claim 78 (new) The method of claim 75, wherein the second portion is fragmented with a methylation-dependent restriction enzyme.

Claim 79 (new) The method of claim 71, wherein the methylated DNA is depleted from the randomly cleaved or sheared DNA.

Claim 80 (new) The method of claim 71, wherein the unmethylated DNA is depleted from the randomly cleaved or sheared DNA.

Claim 81 (new) The method of claim 71, wherein the quantification step comprises hybridizing the DNA depleted for methylated or unmethylated DNA to a nucleic acid linked to a solid support.

Claim 82 (new) The method of claim 81, wherein the solid support is selected from the group consisting of a microarray, a bead and a matrix.

Claim 83 (new) The method of claim 71, wherein the organism is selected from a plant, an animal, a fungus, and a prokaryote.

Claim 84 (new) The method of claim 83, wherein the prokaryote is selected from a group consisting of a gram negative bacterial pathogen, a gram positive bacterial pathogen, and mycobacteria.

Claim 85 (new) The method of claim 83, wherein the animal is a human.

Claim 86 (new) The method of claim 71, wherein the cell is a stem cell.

Claim 87 (new) The method of claim 71, wherein the cell is a transgenic cell and the nucleic acid corresponds to the insertion site of a transgene.

Claim 88 (new) The method of claim 71, wherein the tissue is selected from the group consisting of blood, biopsy tissue, resected tissue, normal tissue, tumor tissue and precancerous tissue.

Claim 89 (new) The method of claim 71, wherein the method further comprises comparing the methylation profile of a nucleic acid with a transcription profile of the nucleic acid, thereby determining the relation between methylation profile and the transcription profile of the nucleic acid.

Claim 90 (new) The method of claim 89, wherein the transcription profile of the nucleic acid is detected with a microarray.

Claim 91 (new) The method of claim 71, further comprising comparing the methylation profile of a specimen of a bacterial pathogen with a reference strain of the pathogen, wherein similarity of the methylation patterns indicates common origin of the specimen and the reference strain.

Claim 92 (new) The method of claim 71, wherein the average size of the uniform population of randomly cleaved or sheared DNA is between 0.1-10 kb.

Claim 93 (new) The method of claim 71, further comprising comparing the methylation profile of the nucleic acid with the copy number of the nucleic acid, thereby determining the contribution to a phenotype of the combination of the methylation of the nucleic acid and the copy number of the nucleic acid.

Claim 94 (new): The method of claim 93, wherein the copy number of the nucleic acid is detected with a microarray.

Claim 95 (new): The method of claim 71, wherein the quantifying step comprises quantitative amplification.

Claim 96 (new) A method for comparing the methylation profile of at least a first and a second DNA sample, wherein the DNA samples are from at least two different cells, tissues or organisms, the method comprising the steps of:

 a. providing a uniform population of randomly cleaved or sheared DNA from DNA samples;

b. depleting methylated or unmethylated DNA from the randomly cleaved or sheared DNA of the first DNA sample and optionally depleting methylated or unmethylated DNA from the cleaved or sheared DNA of the second DNA sample; and

c. comparing the amount of at least one sequence from the depleted first DNA sample with the amount of the sequence in the cleaved or sheared second DNA sample or the depleted second sample.

Claim 97 (new) The method of claim 96, wherein the depleting step comprises:
 fragmenting the randomly cleaved or sheared DNA with a methylation-sensitive or methylation-dependent restriction enzyme to produce DNA fragmented by the restriction enzyme and DNA unfragmented by the restriction enzyme; and
 separating the fragmented DNA from the unfragmented DNA.

Claim 98 (new) The method of claim 97, further comprising:
 labeling the unfragmented DNA with a label;
 hybridizing the labeled DNA to a nucleic acid; and
 determining the methylation state of the nucleic acid by detecting the labeled DNA hybridizing to the nucleic acid.

Claim 99 (new) The method of claim 96, wherein the methylated DNA is depleted from the randomly cleaved or sheared DNA.

Claim 100 (new) The method of claim 96, wherein the unmethylated DNA is depleted from the randomly cleaved or sheared DNA.

Claim 101 (new) The method of claim 96, wherein the average size of the uniform population of randomly cleaved or sheared DNA is between 0.1-10 kb.

Claim 102 (new): The method of claim 96, wherein the quantifying step comprises quantitative amplification.

Claim 103 (new) The method of claim 96, wherein the quantification step comprises hybridizing the DNA depleted for methylated or unmethylated DNA to a nucleic acid linked to a solid support.

Claim 104 (new) The method of claim 103, wherein the solid support is selected from the group consisting of a microarray, a bead and a matrix.

Claim 105 (new) The method of claim 96, wherein the samples each comprise a first portion and a second portion and the second portion from each sample is contacted with a methylation-sensitive or methylation-dependent restriction enzyme; and

the first portion from the first sample, the second portion from the first sample, the first portion from the second sample and the second portion from the second sample are each labeled with a different label and hybridized to a nucleic acid, wherein the ratio of the hybridization of the first portions provides a CGH profile and the ratio of the hybridization of the first and second portions for each sample provides a methylation profile for each sample.

Claim 106 (new) The method of claim 96, wherein the samples each comprise a first portion and a second portion and the second portion from each sample is contacted with a methylation-sensitive or methylation-dependent restriction enzyme; and

two portions are labeled with different labels and hybridized to a nucleic acid, wherein the two portions are either:

the first portion from the first sample and the second portion from the first;

the second portion from the first sample and the first portion from the second sample;

the first portion from the second sample and the second portion from the second sample; or

the second portion of the second sample and the first portion of the first sample.